Passive Smoking and Heart Disease

Mechanisms and Risk

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Objective.—Recent clinical, laboratory, and epidemiological evidence that passive smoking causes heart disease was reviewed, with particular emphasis on understanding the underlying physiological and biochemical mechanisms.

Data Sources.—Publications in the peer-reviewed literature were located via MEDLINE, citation in other relevant articles, and appropriate reports by scientific agencies. Greatest emphasis was given to work published since 1990.

Conclusions.—Passive smoking reduces the blood's ability to deliver oxygen to the heart and compromises the myocardium's ability to use oxygen to create adenosine triphosphate. These effects are manifest as reduced exercise capability in people breathing secondhand smoke. Secondhand smoke increases platelet activity, accelerates atherosclerotic lesions, and increases tissue damage following ischemia or myocardial infarction. The effects of secondhand tobacco smoke on the cardiovascular system are not caused by a single component of the smoke, but rather are caused by the effects of many elements, including carbon monoxide, nicotine, polycyclic aromatic hydrocarbons, and other, not fully specified elements in the smoke. Nonsmokers exposed to secondhand smoke in everyday life exhibit an increased risk of both fatal and nonfatal cardiac events.

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IN 1991, we reviewed the available epidemiological, clinical, physiological, and biochemical evidence, and concluded that environmental tobacco smoke (ETS) caused heart disease in nonsmokers.[1] We estimated that ETS contributed about 37 000 heart disease deaths to the total of 53 000 annual deaths due to ETS, making passive smoking the third leading preventable cause of death, after active smoking and alcohol. Since then, there have been several other reviews of the literature that have reached similar conclusions,[2-6] and the American Heart Association has concluded that passive smoking is an important risk factor for heart disease in both adults[7] and children.[8] The Occupational Safety and Health Administration included the effects of ETS on the heart in its risk assessment of passive smoking as part of a proposed rule that workplaces be essentially smoke-free.[9] This article updates our earlier review,[1] with particular emphasis on new information that provides a clearer understanding of the mechanisms by which passive smoking causes heart disease.

EFFECTS OF ETS ON OXYGEN DELIVERY, PROCESSING, AND EXERCISE

Passive smoking reduces the blood's ability to deliver oxygen to the myocardium. The carbon monoxide in ETS displaces and competes with oxygen for binding sites on red blood cells.[10-14] Children of smoking parents have elevated levels of 2,3-diphosphoglycerate, an enzyme that increases the disassociation of oxygen from hemoglobin in red blood cells in an effort to compensate for chronic oxygen deprivation.[5,12,15-17] While the reduction in oxygen-carrying capacity of blood caused by increased carboxyhemoglobin is small compared with smokers, it can have important physiological implications because the body normally extracts more than 90% of the oxygen from the blood during exercise.[18] People with existing heart disease show increasing electrocardiographic evidence of ischemia[19,20] and experience more arrhythmias[21] as carboxyhemoglobin increases, even at low levels.

In addition to reducing the blood's ability to deliver oxygen to the heart, there is direct evidence from animal studies that passive smoking reduces the ability of the heart muscle to convert oxygen into the "energy molecule" adenosine triphosphate. In a study in rabbits, the activity of the mitochondrial enzyme cytochrome oxidase fell 25% after a single 30-minute exposure to secondhand smoke, and the activity continued to decline with prolonged exposure.[22] After 8 weeks of exposure of 30 minutes per day, its activity was reduced by half. Thus, not only does secondhand smoke reduce the ability of the blood to deliver oxygen to the myocardium, but it also reduces the ability of the myocardium to effectively use the oxygen it receives.[23]

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Passive smoking has also been shown to significantly increase the amount of lactate in venous blood, which indicates that during passive smoking the heart increasingly relies on anaerobic metabolism.[24] People with coronary heart disease cannot exercise as long or reach as high a level of exercise after breathing secondhand smoke than when breathing clean air[14,25,26] and are more likely to develop arrhythmias with exercise.[27] Healthy young adults exposed experimentally to secondhand smoke show higher resting heart rates, higher blood carboxyhemoglobin levels, a significant reduction in the amount of oxygen absorbed during exercise, and a shorter time to exhaustion when running on a treadmill.[14,24] These studies also demonstrated an increased perceived level of exertion during exercise and an increase in maximum heart rate, carbon dioxide output, and the time to recover resting heart rate at the end of exercise, to the point that normal healthy individuals took as long as people with heart disease to recover their resting heart rate following exercise.[14,24]

PLATELETS

Secondhand cigarette smoke activates blood platelets, which increases the likelihood of formation of a thrombus and can damage the lining of the coronary arteries and facilitate the development of atherosclerotic lesions.[28-33] Large platelets and mean platelet volume are independent risk factors for recurrent or more serious myocardial infarction.[34]

In one experiment, nonsmokers and smokers were asked to smoke two cigarettes.[31] The smokers' platelets, which were more active than the nonsmokers' platelets at the beginning of the experiment, did not significantly change activity in response to the two cigarettes. Most likely, the smokers' platelets were maximally activated because of the chronic exposure to the toxins in cigarette smoke, so the addition of the relatively small (compared with what a smoker receives on an ongoing basis) amount of toxins in two cigarettes had no additional effects. In contrast, smoking just two cigarettes significantly increased nonsmokers' platelet activity, to the point that it was not significantly different from that of habitual smokers. This situation demonstrates that the responses of nonsmokers and smokers to toxins in the cigarette smoke are often very different.

In an experiment that more closely paralleis the experience of nonsmokers, the same investigator[31] measured platelet activity in smokers and nonsmokers before and after they sat in a room for 20 minutes where cigarettes had been smoked just before the experimental subjects entered. Again, there was no significant change in the platelet activity among the smokers, but a significant increase in platelet activity among the nonsmokers, to the point that their platelet activation was not discernibly different from the smokers. These data, together with other human experiments,[29,35-38] indicate that nonsmokers are much more sensitive to secondhand smoke than smokers and that very low levels of ETS exposure can have major impact on nonsmokers' platelet activity. It also appears that the process saturates at low doses: once the nonsmoker has been exposed to even a low dose of secondhand smoke, the platelets are maximally activated, similar to that of a habitual smoker. These data also indicate that dose-based extrapolations from smokers to nonsmokers using "cigarette equivalents" will grossly underestimate the risks to nonsmokers of breathing secondhand smoke.

Animal data also support this conclusion. In our studies of the effects of passive smoking on heart disease, we have found that bleeding time, another measure of platelet activity, is significantly shortened (meaning more activated platelets) in both rabbits[39,40] and rats[41] exposed to low doses of secondhand smoke, with no additional effects at higher doses.

At a biochemical level, studies of cigarette-smoke extract on the effects of platelet activity suggest that the toxins in the cigarette smoke increase platelet-activating factor by interfering with the activity of the plasma enzyme platelet-activating factor acetylhydrolase,[42] which reduces platelet activity by neutralizing platelet-activating factor. Because toxins in the cigarette smoke appear to reduce the effectiveness of platelet-activating factor acetylhydrolase in neutralizing platelet-activating factor, these toxins may contribute to an increase in platelet activity. Nicotine does not appear to be the only active agent in tobacco smoke; some other as-yet-undefined element in the smoke also contributes to these effects on the platelets.[36,42] This biochemical result is reinforced by clinical studies that find that smokers treated with nicotine patches show fewer changes in platelet activity than continuing smokers despite having similar nicotine levels.[43]

ATHEROSCLEROSIS

In addition to short-term toxic effects of cigarette smoke, there are long-term permanent effects. In particular, smoking contributes to the development of atherosclerosis. In addition to their role in acute thrombus formation, platelets are also important in the development of atherosclerosis.[33,44] Once there is damage to the arterial endothelium through mechanical or chemical factors, platelets interact with or adhere to the subendothelial connective tissue and initiate a sequence that leads to formation of atherosclerotic plaque. When platelets interact with or adhere to subendocardial connective tissue, they are stimulated to release their granule contents. Endothelial cells normally prevent platelet adherence because of the nonthrombogenic character of their surface and their capacity to form antithrombotic substances such as prostacyclin. Once the endothelial cells have been damaged, the platelets adhere and release mitogens such as platelet-derived growth factor, which encourages migration and proliferation of smooth-muscle cells in the region of the endothelial injury. If platelet aggregation is increased because of exposure to ETS, the likelihood that platelets will adhere at that endothelial injury site will be increased.

Experiments in humans have indicated that even short-term exposure to ETS—like active smoking[45]—significantly increases the appearance of anuclear endothelial cell carcasses in the blood of people exposed to ETS (or other tobacco products) constituents.[29] The appearance of these cell carcasses indicates damage to the endothelium, which is the initiating step in the atherosclerotic process. The appearance of these cells after passive smoking in nonsmokers is almost as great as in active smoking in nonsmokers.[29]

Passive smoking both among adolescents whose parents smoke and also in adults working in places where smoking is permitted exhibit lower levels of high-density lipoprotein than children breathing clean air.[12,17] Similar results have been reported in adults who work in smoky environments.[46] This effect on cholesterol and the ratio of high-density lipoprotein to total cholesterol contributes to the risk of developing atherosclerosis.

Many atherosclerotic plaques in humans are either monoclonal or possess a predominantly monoclonal component, which indicates that the smooth-muscle cells of each plaque have a predominant cell type. Several animal studies, reviewed previously,[1] demonstrated that polycyclic aromatic hydrocarbons, in particular 7,12-dimethylbenz(a,h)anthracene and benzo(a)pyrene, accelerate the development of atherosclerosis. Benzo (a)pyrene is an important constituent of ETS. The polycyclic aromatic hydrocarbons appear to bind preferentially to both the low-density lipoprotein and high-density lipoprotein subfragments

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of cholesterol, which may facilitate incorporation of the carcinogenic compounds into the cells lining the coronary arteries and hence contribute to both cell injury and hyperplasia in the atherosclerotic process.

In addition to this biochemical evidence demonstrating the effects of specific components in ETS on the development of atherosclerotic lesions at a cellular and molecular level, recent *animal* experiments have demonstrated that short-term exposure to ETS significantly speeds the atherosclerotic process. Zhu et al[39] exposed three groups of rabbits on a high-cholesterol diet to secondhand smoke 6 hours a day, 5 days a week for 10 weeks. The low-dose group was exposed to smoke at levels that would be observed in a smoky bar, whilethe high-dose group was exposed to pollution levels comparable with those observed in an automobile with the windows rolled up and four cigarettes per hour being smoked.[47] After the relatively short period of 10 weeks or 300 hours of exposure, the fraction of pulmonary artery and aorta covered with lipid deposits doubled.

This effect appears to be directly caused by elements in the cigarette smoke itself, rather than a reaction to the ETS that might have increased circulating catecholamines. (Increased levels of circulating catecholamines is one of the mechanisms by which cigarette smoking increases the risk of heart disease in active smokers.) Sun et al[40] exposed rabbits, in an experiment similar to that just described, to secondhand smoke, but gave half the rabbits the β-blocking drug metoprolol. As expected, the animals receiving metoprolol developed fewer lipid deposits than those who were receiving saline placebo, but this effect was independent of whether the rabbits were breathing secondhand smoke. Therefore, the effects of ETS on the development of arterial atherosclerosis was not mediated by the increased levels of catecholamines.

One criticism has been that this rabbit model of atherosclerosis requires the rabbits to be on a high-cholesterol diet.[48] This experimental model of atherosclerosis, which has been used since 1908, requires the rabbits to have a high-cholesterol diet in order to develop any lesions within a reasonable length of time.[49] However, Penn et al[50,51] showed similar increases in plaque development in young cockerels (between 6 and 22 weeks old) who were exposed to secondhand smoke 6 hours a day, 5 days a week for 16 weeks. The cockerels were exposed to lower levels of secondhand smoke than the rabbits and were eating a normal, low-cholesterol diet. There was a significant acceleration in the growth of atherosclerotic plaques associated with passive smoking.

After publication of the first study by Penn et al,[50] the tobacco industry protested that the exposure levels were "unrealistically high," and urged them—through its Center for Indoor Air Research, which funded Penn's work—to repeat the experiment at lower levels of exposure.[52] Penn et al[51] conducted a second study, in which the cockerels were exposed to the smoke from a single cigarette at a time, yielding ETS pollution levels comparable to or below levels observed in bars. The second study produced results similar to the first: ETS accelerated the development of atherosclerotic plaque. The Center for Indoor Air Research has refused to continue funding any more work by Penn on this subject (written communication to Susan Sherman regarding Gio Gori's testimony before the Occupational Safety and Health Administration, January 2, 1995).

The carcinogens in smoke appear to be acting as a promoter to facilitate the development of plaques, rather than an initiator of plaques.[52] In addition, it is unlikely that these effects are caused by the carbon monoxide in the smoke, because other experiments where cockerels were exposed to high doses of carbon monoxide did not produce similar effects. In contrast, exposure to secondhand smoke for a relatively brief time (corresponding to about 0.4% of their life span) significantly accelerated the development of plaques. The fact that it is possible to induce atherosclerotiClike changes in two different species of experimental animals with only a few weeks' exposure to secondhand smoke similar to that experienced by people in normal day-to-day life, is an important finding linking the epidemiological and biochemical evidence that passive smoking causes heart disease. The experimental studies on rabbits and cockerels, which do not suffer from the gap created by potential confounding variables in epidemiological studies, bridge this gap by showing that it is possible to induce atherosclerosis in experimental animals with ETS.

Finally, there are also population-based data in humans showing that passive smokers have significantly thicker carotid artery walls, in a dose-response relationship, than people who never were exposed to passive or active smoking.[53] The increased carotid intimal-medial thickness persisted even after controlling for differences in diet, physical activity, body mass index, alcohol intake, education, and major cardiovascular risk factors. At the midrange age of the study population (55 years), the increase in intimal-medial thickness for passive smokers was 23% of that observed in active smokers, despite the fact that the dose of tobacco smoke absorbed by passive smokers is much less than that absorbed by active smokers. This relatively large effect (compared with the dose) is consistent with what one would expect from the animal studies and is consistent with the comparable relatively large effect of ETS on the risk of heart disease mortality and morbidity observed in epidemiological studies.

FREE RADICALS IN ETS AND ISCHEMIC DAMAGE

Free radicals are highly reactive oxygen products[54,55] that are extremely destructive to the heart muscle cell membrane as well as other processes within the cell. Passive smoking worsens the outcome of an ischemic event in the heart through the activity of free radicals during reperfusion injury; low exposures to nicotine or other cigarette smoke constituents significantly worsen reperfusion injury.

The nicotine of just one cigarette doubled the reperfusion injury in dogs.[56] This is so low a dose of nicotine that it had no effect on the dogs' heart rate, blood pressure, regional myocardial shortening, or other hemodynamic measures of cardiac function. These parameters are commonly affected by nicotine in active and passive smokers.[57] After an ischemic episode in which the left anterior descending coronary artery was ligated for 15 minutes, the regional shortening during reperfusion was reduced by 50% of the preischemic values. When the dogs were exposed to the nicotine from one cigarette, the muscle shortened by 25% of control values. When the dogs were given a free radical scavenger with the nicotine, this effect was obliterated. Thus, exposure to a very low dose of nicotine doubled the impact of the reperfusion injury.

The effects of free radicals induced by passive smoking have been explored at the cellular level.[58,59] Rats who were exposed to secondhand smoke from two cigarettes a day for 2 months exhibited severely damaged mitochondrial function during reperfusion injury. The ability of cardiac mitochondrial cells to convert oxygen into adenosine triphosphate was much more compromised during reperfusion injury among rats exposed to low doses of secondhand smoke than among control rats. This is another mechanism by which toxins in secondhand smoke interfere with myocardial energy metabolism.

Smokers may be less sensitive to free radical damage from cigarette smoke than nonsmokers because of changes in

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the levels of enzymes that control free radicals.[60] When hamsters were exposed to the ETS from six cigarettes a day for 8 weeks, the activity of antioxidant enzymes in their lungs nearly doubled. Similar changes were found in the lungs of smokers compared with nonsmokers. Thus, chronic exposure to cigarette smoke appears to increase the free radical scavenging systems in smokers, a "benefit" that nonsmokers would not have when breathing someone else's smoke.

In addition, passive smoking by humans sensitizes lung neutrophils.[61] As with platelets, neutrophils are an important element of the body's defenses against infection and damage. Inappropriately activated neutrophils, however, release oxidants that can play a role in tissue damage in passive smokers. In a group of passive smokers exposed to just 3 hours of sidestream smoke, there were significant increases in the circulating leukocyte counts and stimulated neutrophil migration. The responses to the exposure to secondhand smoke were greater in nonsmokers than in smokers, again suggesting that the biochemistry of ETS in passive smokers is different than in active smokers, rendering the passive smokers more sensitive to the toxins in ETS.

MYOCARDIAL INFARCTION

There are direct animal data to show that ETS promotes more tissue damage following myocardial infarction. Dogs exposed to secondhand smoke 1 hour daily for 10 days, who were then subjected to blockage of a coronary artery, developed myocardial infarctions that were twice as large as those of controls who breathed clean air.[62] This effect was not caused by elevated circulating levels of nicotine or carboxyhemoglobin, since the infarcts were created the day after the last day of ETS exposure. Zhu et al[41] investigated the effects of ETS exposure on infarct size by exposing rats to secondhand smoke 6 hours a day for 3 days, 3 weeks, or 6 weeks, then occluding the left coronary artery for 35 minutes and reperfusing the artery. Infarct size increased in a dose-dependent fashion, with the longest exposure (180 hours total ETS exposure) yielding infarcts that were nearly twice as large as those in the control group that breathed clean air (Figure 1). There was no evidence of a threshold effect.

Although smokers seem to be less sensitive to effects of passive smoking than nonsmokers, it is important to recognize that even low doses of cigarette smoke can have important effects on smokers. For patients with coronary artery disease, smoking one cigarette significantly increases coronary vascular resistance.[63] Thus, if smoked at a time when demands for oxygen and blood supply to the heart are increasing,[57,64] even a single cigarette can dramatically reduce the ability of smokers' coronaries to transmit blood. In addition, in habitual smokers smoking a single cigarette, compliance of coronary arterial walls is reduced and may increase the likelihood of rupture of atherosclerotic plaque, an important element in myocardial infarction.[65] It is likely that low doses of cigarette smoke will have similar effects in passive smokers.

EPIDEMIOLOGICAL STUDIES

Wells[5] summarized 12 studies (counting end points for men and women separately even if they were reported in the same article, since cardiovascular risk is different for men and women and effects of passive smoking may differ) that examined heart disease mortality associated with passive smoking (seven studies of nonsmoking women married to men who smoke[66-74] and five of nonsmoking men married to women who smoke[67,69-73,75]). (Two other studies were excluded because they were published only as abstracts,[76,77] but they also showed an increased risk. The fact that the only known unpublished data on passive smoking and heart disease are positive is evidence against the claim[78-80] that there is a publication bias against negative studies on ETS.) Of these 12 studies, 11 show an elevation in risk of death from heart disease for nonsmokers married to smokers (Figure 2) after controlling for other risk factors for ischemic heart disease. Wald,[81] in his analysis of passive smoking and lung cancer, made the point that one can do a simple analysis of the results of multiple epidemiological studies by simply counting the studies that show relative risks (RRs) above and below 1.0. The probability of observing 11 of 12 studies with an increased risk by chance if passive smoking did not affect the risk of heart disease death is only .003. In addition, eight of these studies show a positive dose-response relationship. These results are consistent with the conclusion that passive smoking increases the risk of heart disease death.

Wells[5] pooled the results from all 12 studies using the same approach as the US Environmental Protection Agency to estimate the effects of passive smoking and lung cancer.[82] Pooling resulted in an RR for dying of heart disease of 1.2 (95% confidence interval [CI], 1.1 to 1.4). Therefore, we can be more than 95% confident that passive smoking affects the risk of dying from heart disease and more than 97.5% confident that passive

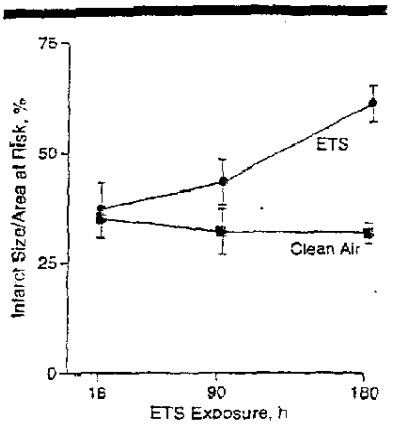

Figure 1.—The effect of passive smoking on infarct size in rats subjected to a 35-minute occlusion of the left coronary artery (from Zhu et al[41]). Infarct size increases in a dose-dependent manner without a threshold effect. ETS indicates environmental tobacco smoke; data are means with SE bars.

smoking increases the risk of death from heart disease. Applying this risk on a population basis yields an estimated 62 000 heart disease deaths in 1985,[5] compared with only 3000 from lung cancer.[83] Because of declines in smoking and increases in smoke-free environments, Wells[5] estimates that this toll would have fallen to 47 000 by 1994.

When Wells[5] limited his analysis to the five studies that best controlled for confounding variables for heart disease deaths, he obtained a higher adjusted RR for passive smoking and heart disease mortality of 1.7 (95% CI, 1.3 to 2.3). Therefore, the more potentially confounding factors were controlled for, the higher the risk that Wells found attributed to secondhand smoke. The tobacco industry often criticizes studies for failing to account for confounding variables[83] on the grounds that failure to account for confounders artificially inflates the observed RR and makes it appear that ETS is more dangerous than it really is. Wells found just the opposite result.

In addition to the epidemiological studies that used death as an end point, there are also 11 studies (considering men and women separately) that examined nonfatal cardiac disease (Figure 3), such as a nonfatal myocardial infarction, presence of angina, or malignant electrocardiographic changes.[67,69,75,84-88] Nine of these studies show an elevation in risk. The probability of observing nine positive studies out of 11 if there was no effect of passive smoking on nonfatal cardiac events is only .03. Wells' formal analysis (written communication, August 1994) to pool these studies yields a RR for nonfatal coronary events associated with exposure to secondhand smoke of

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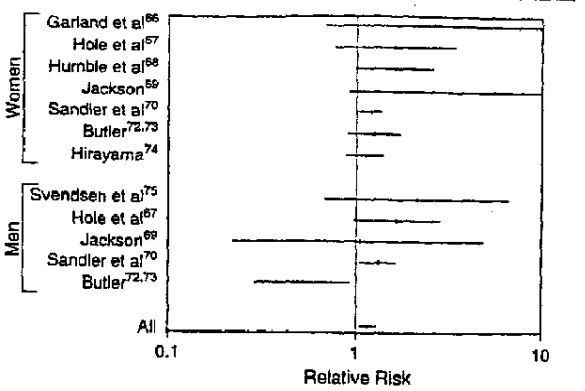

Figure 2.—The effect of passive smoking on the risk of fatal myocardial events from published epidemiological studies.[66-70,72-75] Pooled risk estimates include all studies as determined by Wells.[5] Horizontal bars indicate 95% confidence intervals; upper bounds are off the scale for the Garland et al[66] and Jackson[69] studies.

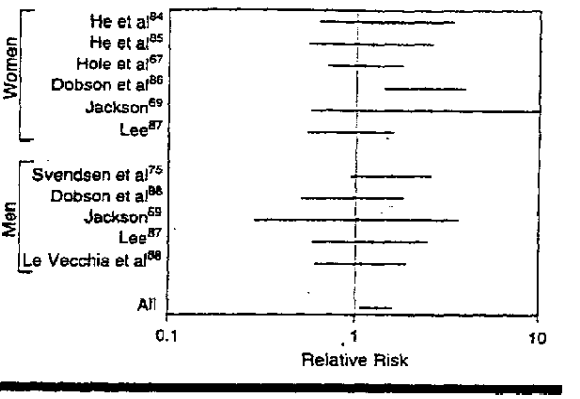

Figure 3.—The effect of passive smoking on the risk of nonfatal myocardial events from published epidemiological studies.[67,69,75,84-88] Pooled risk estimates are from Wells (written communication, August 1994) and include the data from LaVecchia et al,[88] which was not available for the published[5] computations. Horizontal bars indicate 95% confidence intervals; upper bounds are off the scale for the Jackson[69] study.

1.3 (95% CI, 1.1 to 1.6). Three of these studies show a dose-response relationship, with higher exposures of secondhand smoke associated with larger increases in risk. The fact that passive smoking increases the risk of nonfatal coronary events as well as fatal coronary events is consistent with what we know about the physiology and biochemistry of how passive smoking affects the heart.

Some of these studies used marriage to a current smoker as the measure of exposure to ETS,[68-71,75-77,86] whereas others used marriage to an ever-smoker (even if the spouse was currently a nonsmoker) as the measure of exposure to ETS.[66,67,72-74,84,85,87,88] Given the fact that the effects of smoking (and, presumably, passive smoking) on the heart decline quickly[89] when exposure ends, the design of these studies is often biased against detecting an effect of ETS on heart disease. In addition, the fact that the observed risks are of comparable magnitude across studies done in many countries and controlling for a variety of the other risk factors for heart disease strengthens the confidence one can have in reaching a conclusion that passive smoking causes heart disease.

CONCLUSION

The ability of the heart and vascular system to adapt to changing conditions is an important factor when considering the health effects of ETS, particularly when one compares the effects of ETS in nonsmokers with smokers. People who smoke cigarettes are chronically and continually adversely affecting their cardiovascular system,[10] which adapts to compensate for all the deleterious effects of smoking. Nonsmokers, however, do not have the "benefit" of this adaptation, so the effects of passive smoking on nonsmokers are much greater than on smokers. This difference probably arises for two reasons: first, nonsmokers' hearts and vascular systems have not attempted to adapt to the chemicals in secondhand smoke. Second, it appears that the cardiovascular system is extremely sensitive to many of the chemicals in secondhand smoke. Smokers may have achieved the maximum response possible to at least some of the toxins in the smoke, so the small additional exposures associated with passive smoking have little or no effect on habitual smokers because the additional dose of these toxins is small compared with what the smoker normally receives.

These two facts make it imperative to consider the effects of ETS on the cardiovascular system of passive smokers separately from the effects on active smokers. The qualitative differences between the effects of ETS on smokers and nonsmokers explain the high RRs associated with passive smoking compared with active smoking, even though passive smokers absorb much smaller doses of the toxins in cigarette smoke than smokers do.[90] In particular, the practice—often advocated by the tobacco industry and its scientific consultants when considering secondhand smoke—of thinking about "cigarette equivalents" or simple dose-based extrapolations from smokers to nonsmokers will lead to gross underestimations of the risks of passive smoking to the cardiovascular system. Tobacco industry proponents frequently state that even a heavily exposed passive smoker breathes in the equivalent of less than one cigarette per day.[83] This assertion ignores the complex chemistry of ETS; some toxins in ETS are higher than in smoke inhaled by smokers, some are lower.[11,82,91] The tobacco industry justifies this assertion by using chemicals that are relatively rich in mainstream smoke compared with ETS using some of the carcinogens in ETS yields the equivalent of several cigarettes a day.[83] In any event, leaving aside the philosophical question of whether anyone ought to be required to breathe even one cigarette a day under any circumstances, the ETS experienced by many people in their daily lives is enough to produce substantial adverse effects on the cardiovascular system.

Using different methodologies, several investigators have estimated the population burden associated with passive smoking and heart disease, yielding estimates of 30 000 to 60 000 deaths annually in the United States,[1,2,5,92] with about three times as many nonfatal cardiovascular events. This is a tremendous public health impact and one that warrants strong action, commensurate with that devoted to health problems that affect a smaller percentage of the population such as illegal drugs and the acquired immunodeficiency syndrome,[93] to protect workers, children, and the general public. The simplest and most cost-effective control measure is to mandate smoke-free workplaces, schools, and public places.[9,83,94-98]

This article is based on testimony presented before the Occupational Safety and Health Administration on September 21, 1994, in support of its proposed Indoor Air Quality rule.[9] The Occupational Safety and Health Administration partially supported Dr Glantz for time spent preparing that testimony.

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